APPENDIX N: Statements of Dissent

The ReMAP Task Force strived to achieve unanimity in this report. In the second meeting of the Task Force, on April 22, all but one Task Force member agreed to the priority ranking of the research. Well after the third and final meeting of the Task Force on May 17, further dissent developed, both before and after the ReMAP report was presented on July 10 to the NASA Advisory Committee and the public. The dissenters were invited to write Minority Opinions and/or Statements of Dissent, which are included here. See also Appendix C, charts 66 – 68.

June 4, 2002
COMMENTS ON ReMAP'S FINDINGS AND RECOMMENDATIONS

As a member of the OBPR Research Maximization and Prioritization (ReMAP) Task Group I wish to express my concerns about:

1. The process by which priorities for microgravity research programs were assigned, and

2. The ranking given to the protein crystallization program.

THE PRIORITIZATION PROCESS

From my observations the process used by ReMAP in setting priorities for microgravity research was so biased, superficial and arbitrary as to cast serious doubts on the validity of the panel's findings and recommendations. I believe this came about for the following reasons:

Composition of the Task Group

The selection of the members of ReMAP was biased toward small animal studies and to the proposition that life in space, rather than life on earth, should be the principal rationale for microgravity research.

Many members of the task group had little or no previous experience with NASA's research programs. Perhaps it was intended that this would ensure a fresh outlook but in practice this lack of historical perspective led to less informed decision-making.

Although many of the programs evaluated had a medical or commercial rationale, only a few members of the panel had the requisite expertise to evaluate them.

Time Constraints

The task group was called upon to prioritize current or proposed microgravity research programs in 8 categories, which were divided into 41 programs, many of which were in turn divided into several subprograms. Only two days were allowed for this exercise. The prioritization process was so rushed and the volume of information to digest so voluminous that most programs were evaluated only superficially.

The research programs ReMAP was asked to consider all fall naturally into one of three categories:

1. Human Health and Safety Research
2. Biological and Physical Research
3. Commercial Research

An inordinate amount of time was spent discussing programs in the first category even though all agreed that the health and safety of the crew is of the highest priority. A separate panel of experts in space medicine should have prioritized the programs within this category.

Commercial research was given very short shrift by the task group composed, as it was, mainly of individuals with no industrial experience. A separate panel, of scientists from industry, should have prioritized the programs within this category.

Had the work of ReMAP been divided into three separate, concurrent panels, the discussions would have been more substantive and the prioritization process more valid. There is no need to prioritize among the three categories, because the first is undisputedly a top priority and Congress mandates the third.

Lack of Attention to Previous Peer Reviews

Since there was no time to develop independent evaluations of research programs, previous peer reviews should have been accepted as the basis for setting priorities. This was certainly not done in the case of the protein crystallization program.

Several members who had no previous experience with the program or expertise in crystallography expressed strong negative opinions about its worth. From their comments it was clear that these individuals based their opinions on criticisms they had heard from persons outside the task group.

However, these criticisms were all addressed by a recent NRC report [*Future Biotechnology Research on the International Space Station*, National Academy Press, Washington, D.C., (2000)]. NASA has moved expeditiously to implement the NRC recommendations.

Only three members of ReMAP stated that they had ever seen or read the NRC report. I requested that copies of the report be distributed to all the members before the final meeting, but this was not done. To the extent that the NRC report was considered at all, it was misrepresented and quoted out of context.

Failure to Adhere to a Consistent Set of Prioritization Criteria

The ranking process was arbitrary and chaotic. At the first meeting ReMAP members were given a list of NASA criteria to be used in evaluating the research programs. However, these metrics were totally ignored. No research program was ever formally graded according to that set of criteria or any other.

The prioritization of programs in each of the eight categories was carried out in breakout groups. Any ReMAP member was free to participate in any breakout group, no matter what his or her degree of expertise in the field. The discussions were brief, less than 30 minutes total for all the programs in each category, and tended to be dominated by a few vocal individuals. No votes on rankings were ever taken, even where there was clear disagreement.

RANKING OF THE PROTEIN CRYSTALLIZATION PROGRAM

There is a serious disconnect between reality and the ReMAP findings that ranked protein crystallization in the lower third of all the programs considered.

I believe protein crystallization should be given the highest microgravity science priority on the following bases:

Based on Technical Merit, Accomplishments and Potential

No other program considered by ReMAP has the quantity and quality of favorable attributes:

1. The hypothesis upon which the program rests is sound.
2. The success or failure of any experiment can be easily and precisely determined.
3. The potential social and economic impact of the program is enormous.
4. The program has recently been peer reviewed in great detail.
5. There is a large and supportive user community,
6. Approximately 20% of all proteins flown have shown improvement in crystal diffraction resolution.
7. The program has an impressive record of commercial spin-offs.
8. There have been many fundamental ground-based experiments on protein crystal nucleation and growth.
9. Sophisticated automated experimental hardware has been demonstrated.
10. There is now a very large experimental database available.
11. An extensive educational outreach program has been developed.

Based on NASA's Research Merit Criteria

Since ReMAP ignored the NASA Research Merit Criteria given to us at the first meeting, I have done my own evaluation of the protein crystallization program based on those metrics. I have given each of the 31 criteria listed below a score of 1 to 5, with 1 being the highest.

Giving equal weight to each of the criteria (although clearly some are more important than others) my overall score for the protein crystallization program is 1.8. I doubt that any other scientific program, were it judged by these same metrics, would rank as high.

I. Impact to Broad Scientific and Technological Community.

a. Will the research have significant benefits/applications to ground-based as well as space-based operations involving the basic disciplines or cross-disciplinary interactions?

Improvement in the diffraction resolution of protein crystals can be expected to contribute significantly to fundamental knowledge of biological structures and mechanisms and to the structure-based design of new drugs for human and animal disease and of new chemical agents for the production of food and fiber.
Ranking 1

b. Will the results have broad usefulness, leading to further theoretical, experimental, or commercial and technological developments that have application beyond the particular initiative?

Yes. See I.a. above.
Ranking 1

c. Will the research help demonstrate the benefit of using the environment of space to further the advancement of knowledge or to enhance products and services on Earth?

Yes, the benefit of the microgravity environment has already been shown for at least 36 proteins to yield crystals that diffract to higher resolution than the best grown on earth. It is already NASA's most successful microgravity program.
Ranking 1

d. Is there a potential for stimulation of future technological "spin-offs"?

The Center for Biophysical Sciences and Engineering (CBSE) located at the University of Alabama at Birmingham (a NASA-funded Commercial Space Center) has an impressive commercialization program.

- Four companies have been spun off from CBSE:

(1) Biocryst Pharmaceuticals, a publicly held company listed on NASDAQ, has 77 employees. CBSE has licensed to Biocryst inhibitors of three target enzymes, all of them in clinical trials. CBSE will receive royalties on any drugs marketed by the company.

(2) Diversified Scientific, Inc., is commercializing laboratory crystallization technology developed at CBSE.

(3) Ibbex is developing certain medical and research diagnostics, in collaboration with a member of the CBSE staff.

(4) Oculus Pharmaceuticals is developing high throughput crystallization proteomics technology developed at CBSE.

- CBSE has grown in microgravity crystals of an anti-infective target enzyme that show significantly higher diffraction resolution than the best grown on earth. This has resulted in collaboration with an undisclosed biotechnology company for development of inhibitors of the enzyme.

- In addition, CBSE has supported and/or participated in a number of instrumentation development collaborations with the private sector for technology needed for microgravity experiments.

Ranking 1

e. Will the value of the product if or when it is realized in an application be timely?

This is the biggest challenge the protein crystallization program faces. In order to match the pace of structural biology and drug-design research, the process for growing crystals in microgravity must be speeded up and made more user friendly. The number of crystallization experiments must be greatly increased and crystals must be preserved by cryo-freezing while they are fresh.

Ranking 3

f. Will the research stimulate integration or combination of now separate concepts or information?

Probably not.

Ranking 5

g. Will the research results be applicable or beneficial to an area not immediately related to the field of research?

Possibly. Some hardware developed for protein crystallizations on ISS may be used in analytical and diagnostic testing in ground-based laboratories.

Ranking 3

h. What is the impact on existing international agreements?

The European and Japanese space agencies have an active interest in protein crystallization and have designed and flown apparatus on the Space Shuttle. There are probably other current or potential international collaborations, but I don't know the particulars.

Ranking 1

i. Is there potential for economic impact?

The economic potential is extraordinarily high. The annual sales of many drugs exceed one billion dollars and some are several times that. It is not unreasonable to assume that the lifetime market value of a single important drug designed using data from protein crystals grown in microgravity could exceed the entire cost of the ISS.
Ranking 1

II. Science Importance

a. Are the key scientific questions addressed by the specific research important?

Protein crystallization is of course a means to an end. The end, an understanding of biological structures and mechanisms and the design of drugs, is extraordinarily important.
Ranking 1

b. Does the research represent a groundbreaking advance or is it incremental relative to state-of-the-art?

In most cases the enhancement in diffraction resolution will be incremental. But even incremental improvements in resolution are very important in structure-based drug design research, where one is looking for the position of a smallmolecular needle in a large macromolecular haystack.
Ranking 1

c. Is there a potential for insight into previously unknown phenomena, processes, or interactions?

NASA has already supported a number of ground-based experiments that have yielded important insights into the process of macromolecular crystal nucleation and growth. This body of research is one of the strong points of the program.
Ranking 1

d. Is the research a significant contribution to timely issues, or just buzzword compliant?

Structural biology and drug design are currently two of the hottest areas of scientific inquiry.
Ranking 1

e. Will the research provide powerful new techniques for observing nature?

Although x-ray diffraction is not a new technique, the availability of higher diffracting crystals will certainly improve our picture of nature. If slow diffusion controlled crystal growth of very large macromolecular complexes is as important as many believe, then

microgravity may help open a whole new window on nature, i.e., the structures of integral membrane receptors and membrane-bound complexes.
Ranking 2

f. Will the research answer fundamental questions or stimulate theoretical understanding of fundamental processes or structures?

Yes. See I.a, above.
Ranking 1

g. Is there potential for an important advance in knowledge or understanding in areas at the boundaries between disciplines?

X-ray crystallography is a field which itself spans the boundaries between physics, chemistry and biology. Indeed many of today's structural biologists started their careers in one of those three fields before taking up crystallographic research.
Ranking 1

III. Contributions to National Goals

a. Will the research contribute to national pride and to the image of the United States as a scientific and technological leader because of the magnitude of the challenge, the excitement of the endeavor, or nature of the results?

The United States is already recognized as the world leader in drug research. The protein crystallization program can be expected to contribute to this position.
Ranking 1

b. Will the research contribute to education by generating student interest in science or by attracting students to science and engineering?

NASA has sponsored an exciting educational outreach program in protein crystallization through the University of California at Irvine. Students and teachers, working in their school classrooms and laboratories, are given an opportunity to learn about and to set up crystallizations of some of the same proteins being flown on the Space Shuttle. As of April 2002, more than 50,000 students and 1090 teachers from 320 schools across 36 states and Puerto Rico had participated though workshops and classroom and laboratory activities. Several hundred students and teachers have helped prepare the actual samples for four recent Space Shuttle flights.
Ranking 1

c. Will the research aid in fostering of commercialization of space?

If the protein crystallization facility on International Space Station is as successful and as user friendly as I believe it could be, many pharmaceutical and biotechnology companies are likely to want to participate. There might even be consortia of companies formed to

build and operate facilities for proprietary research on ISS. A model for such a consortium is that formed by twelve pharmaceutical companies to build and operate x-ray beamlines at the Advanced Photon Source synchrotron at Argonne National Laboratory.
Ranking 1

d. Will the research present opportunities for cooperation with external organizations including international partners?

Such cooperation already exists. See I.h. above.
Ranking 1

e. Will the research engage and involve the public in research in space?

NASA's educational outreach program at the University of California at Irvine is an important step in that direction. See III.b. above.
Ranking 1

f. *Will the research contribute to public understanding of the natural world and appreciation of the goals and achievements of science?*

Protein crystallography is one of the most esthetically pleasing of all sciences. Who does not appreciate the beauty of crystals, the symmetry of lattices or the elegance of a protein structure? Modern computers, graphic displays and three-dimensional animation software have made it possible to open to public understanding the world of complex molecular structures and their interactions. But it all starts with crystals that diffract to high resolution.
Ranking 1

g. Will the research benefit the economic health of this nation?

Yes. Vastly more than any other microgravity research yet proposed. The U. S. pharmaceutical industry is one of the biggest positive contributors to the nation's balance of trade. See also I.i. above.
Ranking 1

IV. Vital to NASA's Mission

a. Will the research substantially contribute to the health, safety, and performance of humans living and working in space?

Yes, in the same way that it will benefit all humans.
Ranking 3

b. Will the research enhance ISS productivity?

Possibly, through the development of robotics and remote visualization hardware and software that might be applicable elsewhere on ISS.
Ranking 3

c. Is the space environment of fundamental importance to the research, either in terms of unmasking effects hidden under normal gravity conditions or in terms of using gravity level as an added independent parameter, or in providing access to conditions not available on Earth?

Absolutely. The rationale for growing protein crystals in microgravity is based on the hypothesis that such crystals will be more highly ordered and therefore diffract x-rays to higher resolution. As a crystal grows it depletes the solute in the surrounding solution, creating what is known as a 'depletion zone' around the crystal.

On earth the less dense depletion zone continually dissipates due to the mixing with the higher density bulk solution. This disruption of the equilibrium around the growing crystal results in some solute molecules being laid down in a disordered manner.

In microgravity, however, there is little disruption of the depletion zone. Solute molecules from the bulk solution diffuse slowly through the zone and are laid down on the growing crystal in a more ordered manner.
Ranking 1

d. Will the research substantially contribute to the safety and effectiveness of robotic exploration missions?

No.
Ranking 5

e. Does the research require a NASA-unique ground-based facility or expertise?

NASA has assembled an excellent support staff at Marshall Space Flight Center and funded private companies and university laboratories to assist investigators in flying samples on Space Shuttle.
Ranking 3

f. Does the research advance and communicate scientific knowledge and understanding of the Earth, the solar system, or the universe?

Not specifically about the earth itself, but certainly about life on earth.
Ranking 3

g. Does the research expand advanced aeronautics, space science, or space technology?

No.

Ranking 5

h. Does this research support NASA's goal to foster the commercial use of space?

Very strongly! See I.a., I.d. and I.i. above.
Ranking 1

I have made no attempt to rank the protein crystallization program on NASA's Implementation Criteria since most of these depend on budget and schedule projections that are currently undetermined or are unknown to me.

Noel D. Jones, Ph.D.
June 4, 2002

July 23, 2002
DISSENT FROM THE ReMAP TASK FORCE REPORT

The ReMAP process and product are fundamentally flawed, so I must dissent from many of its conclusions. While there are many reasons for my dissent, some of the most fundamental ones are explained below.

The Task Force's primary task was to prioritize research, especially ISS research, to achieve maximum scientific impact. A part of the ReMAP Task Force's membership believes that meaningful scientific research cannot be done within the constraints of Core Complete construction and current shuttle schedules. However, it is my opinion that there is a considerable amount of excellent scientific work in the physical sciences and commercial programs that can be done within Core Complete and with the scheduled shuttle flights, thus fulfilling the mandate to identify good work in an era of fiscal constraints. Much of this work is consistent with the NASA goal of improving life on earth.

The "boxes," or research categories referred to in the ReMAP report were established early and remained unchanged despite vocal opposition by several members of the committee. This use of predefined "boxes" is contradictory to the charge of maximizing and prioritizing research for NASA. The research programs contained within these boxes were reviewed in only a very cursory manner and the relationships between programs were virtually ignored. These "boxes" artificially categorized the research programs and predetermined many of the ReMAP report's conclusions.

An underlying problem with the entire ReMAP process and product is that there was not sufficient time or resources given to the Task Force members to do a proper job of prioritizing the research programs for NASA. Additionally, these constraints limited the ability of the Task Force members to fully participate in reviewing the information, which has been published as ReMAP conclusions.

It is with a great deal of regret that I feel compelled to write this dissent, rather than issue a minority report. However, my concerns are fundamental to what I perceived as my responsibilities as a member of the ReMAP Committee and articulated early in the process, but was not completely reflected in the report.

Signed:

Raymond J. Bula

July 23, 2002
DISSENT FROM THE ReMAP TASK FORCE REPORT

The ReMAP process and product are fundamentally flawed, so we must dissent from its conclusions. While there are many reasons for our dissent, we have explained the most fundamental ones below.

The committee's primary task was to prioritize research, especially ISS research, to achieve maximum scientific impact. A part of the ReMAP committee's membership believes that meaningful scientific research cannot be done within the constraints of Core Complete construction and current shuttle schedules. However, it is our opinion that there is a considerable amount of excellent scientific work in the physical sciences and commercial programs that can be done within Core Complete and with the scheduled shuttle flights, thus fulfilling the mandate to identify good work in an era of fiscal constraints. Much of this work is consistent with the NASA goal of improving life on earth.

The “boxes,” or research categories referred to in the ReMAP report were established early and remained unchanged despite vocal opposition by several members of the committee. This use of predefined “boxes” is contradictory to the charge of maximizing and prioritizing research for NASA. The research programs contained within these boxes were reviewed in only a very cursory manner and the relationships between programs were virtually ignored. These “boxes” artificially categorized the research programs and predetermined many of the ReMAP report’s conclusions.

An underlying problem with the entire ReMAP process and product is that there was not sufficient time or resources given to the committee members to do a proper job of prioritizing the research programs for NASA. Additionally, these constraints limited the ability of the committee members to fully participate in reviewing the information, which has been published as ReMAP conclusions. For example, the entire committee was not given the opportunity to review the narrative sections of the Executive Summary prior to it being presented to the NAC. And finally, the complete final ReMAP report was not distributed to the entire committee in a timely manner for considered review.

It is with a great deal of regret that we feel compelled to write this dissent, rather than issue a minority report. However, our concerns are fundamental to what we perceived as our responsibilities as members of the ReMAP Committee and were articulated early in the process, but were not reflected in the final report.

Signed:

Andreas Acrivos   Patricia Morris
Elaine Oran   Pierre Wiltzius

July 24, 2002
DISSENT FROM THE ReMAP TASK FORCE REPORT

The ReMAP process and product are fundamentally flawed, so I must dissent from its conclusions. While there are many reasons for this dissent, I strongly support the most fundamental ones described below.

The committee's primary task was to prioritize ISS research to achieve maximum scientific impact. A part of the ReMAP committee's membership believes that meaningful scientific research cannot be done within the constraints of Core Complete construction and current shuttle schedules. (Such a statement was even reported in the media.) However, it is my considered opinion that there is a very much excellent scientific work in the physical sciences and commercial programs that can be done within Core Complete and with the scheduled shuttle flights, thus fulfilling the mandate to identify good work in an era of fiscal constraints. Much of this work is consistent with the NASA goal of improving life on earth.

The “boxes,” or research categories referred to in the ReMAP report were established early and remained unchanged despite vocal opposition by several members of the committee. This use of predefined “boxes” is contradictory to the charge of maximizing and prioritizing research for ISS. The research programs contained within these boxes were reviewed in only a very cursory manner and the relationships between programs were virtually ignored. These “boxes” artificially categorized the research programs and predetermined many of the ReMAP report’s conclusions.

An underlying problem with the entire ReMAP process and product is that there was not sufficient time or resources given to the committee members to do a proper job of prioritizing the research programs for ISS. Perhaps more important, these constraints limited the ability of this committee member to fully participate in reviewing the information, which has been published as ReMAP conclusions. For example, the entire committee was not given the opportunity to review the narrative sections of the Executive Summary prior to it being presented to the NAC. And finally, the complete final ReMAP report was not distributed to the entire committee in a timely manner for considered review.

Thus it is with a great deal of regret that I feel compelled to write this dissent, rather than issue a minority report. However, my concerns are fundamental to what I perceived as my responsibilities as a member of the ReMAP Committee. These and many others were articulated in the process, but were not reflected in the final report.

Regretfully,

Harold Metcalf
Professor of Physics and
Distinguished Teaching Professor